

Appl. No. : 09/991,721
Filed : November 13, 2001

AMENDMENTS TO THE CLAIMS

Please amend Claims 1 and 25, and add Claims 28-44 as follows:

1. **(Currently amended)** A tumor cell comprising a vaccinia virus expression vector comprised of a mutation in a tyrosine kinase (TK) gene of the genome of said vaccinia virus to produce a negative TK phenotype and comprised of a mutation in at least one vaccinia virus growth factor (VVGF) gene of the genome of said vaccinia virus to produce a negative VVGF phenotype ~~with a negative thymidine kinase phenotype and a negative vaccinia virus growth factor phenotype~~, wherein said tumor cell is present *in vivo* in a mammal and does not encompass said mammal.
2. **(Previously presented)** The tumor cell of claim 1, wherein said vector further comprises an exogenous nucleotide sequence.
3. **(Previously presented)** The tumor cell of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus thymidine kinase gene containing a deletion of nucleic acid sequence.
4. **(Previously presented)** The tumor cell of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus genome from which a thymidine kinase gene is deleted.
5. **(Previously presented)** The tumor cell of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus thymidine kinase gene containing an insertion of nucleic acid sequence.
6. **(Previously presented)** The tumor cell of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus thymidine kinase gene containing a substitution of nucleic acid sequence.
7. **(Previously presented)** The tumor cell of claim 1, wherein said negative vaccinia virus growth factor phenotype results from at least one vaccinia virus growth factor gene containing a deletion of nucleic acid sequence.
8. **(Previously presented)** The tumor cell of claim 7, wherein said deletion comprises a deletion of the EGF-receptor binding site of said vaccinia virus growth factor gene.
9. **(Previously presented)** The tumor cell of claim 1, wherein said negative vaccinia virus growth factor phenotype results from a vaccinia virus genome from which at least one vaccinia virus growth factor gene is deleted.

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10. **(Previously presented)** The tumor cell of claim 1, wherein said negative vaccinia virus growth factor phenotype results from at least one vaccinia virus growth factor gene containing an insertion of nucleic acid sequence.

11. **(Previously presented)** The tumor cell of claim 1, wherein said negative vaccinia virus growth factor phenotype results from at least one vaccinia virus growth factor gene containing a substitution of nucleic acid sequence.

12. **(Previously presented)** The tumor cell of claim 2, wherein said exogenous nucleotide sequence is selected from the group consisting of tumor suppressor genes, cytotoxic genes, cytostatic genes, cytokines, suicide genes, and antigen encoding genes.

13. **(Previously presented)** The tumor cell of claim 12, wherein said tumor suppressor gene is selected from the group consisting of WT1, p53, p16, Rb, and BRCA1.

14. **CANCELED**

15. **(Previously presented)** The tumor cell of Claim 1, wherein said vaccinia virus expression vector is produced by a virus particle containing a virus genome, wherein expression of said genome produces a vaccinia virus with a negative thymidine kinase phenotype and a negative vaccinia virus growth factor phenotype.

16. **CANCELED**

17. **(Previously presented)** The tumor cell of Claim 1, wherein said vaccinia virus expression vector is constructed such that the gene for *E. coli lacZ* is inserted into the thymidine kinase (TK) or virus growth factor (VGF) site.

18. **(Previously presented)** The tumor cell of Claim 1, wherein said vaccinia virus expression vector is constructed such that the gene for enhanced green fluorescent protein (EGFP) is inserted into the thymidine kinase (TK) or virus growth factor (VGF) site.

19.-24 **CANCELED**

25. **(Currently amended)** A product made by the method of:

providing a vaccinia virus genome and constructing a vaccinia virus expression vector by;

mutating at least one vaccinia virus growth factor gene of said vaccinia virus genome to produce a negative vaccinia virus growth factor phenotype; and

mutating a thymidine kinase gene of said vaccinia virus genome to produce a negative thymidine kinase phenotype; and

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introducing said vaccinia virus expression vector into a tumor cell, wherein said tumor cell is present in vivo in a mammal and does not encompass said mammal.

26. **CANCELED**

27. **(Previously presented)** The tumor cell of Claim 1 wherein said vaccinia virus expression vector is of the WR strain.

28. **(New)** A composition of matter, comprising a vaccinia virus expression vector comprised of a mutation in a tyrosine kinase (TK) gene of the genome of said vaccinia virus to produce a negative TK phenotype and comprised of a mutation in at least one vaccinia virus growth factor (VVGF) gene of the genome of said vaccinia virus to produce a negative VVGF phenotype, wherein said composition is present *in vivo* in a mammalian tumor cell.

29. **(New)** The composition of Claim 28, wherein said composition further comprises an exogenous nucleotide sequence.

30. **(New)** The composition of Claim 28, wherein said negative TK phenotype results from a vaccinia virus thymidine kinase gene containing a deletion of nucleic acid sequence.

31. **(New)** The composition of Claim 28, wherein said negative thymidine kinase phenotype results from a vaccinia virus genome from which a thymidine kinase gene is deleted.

32. **(New)** The composition of Claim 28, wherein said negative thymidine kinase phenotype results from a vaccinia virus thymidine kinase gene containing an insertion of nucleic acid sequence.

33. **(New)** The composition of Claim 28, wherein said negative thymidine kinase phenotype results from a vaccinia virus thymidine kinase gene containing a substitution of nucleic acid sequence.

34. **(New)** The composition of Claim 28, wherein said negative vaccinia virus growth factor phenotype results from at least one vaccinia virus growth factor gene containing a deletion of nucleic acid sequence.

35. **(New)** The composition of Claim 34, wherein said deletion comprises a deletion of the EGF-receptor binding site of said vaccinia virus growth factor gene.

36. **(New)** The composition of Claim 28, wherein said negative vaccinia virus growth factor phenotype results from a vaccinia virus genome from which at least one vaccinia virus growth factor gene is deleted.

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37. (New) The composition of Claim 28, wherein said negative vaccinia virus growth factor phenotype results from at least one vaccinia virus growth factor gene containing an insertion of nucleic acid sequence.

38. (New) The composition of Claim 28, wherein said negative vaccinia virus growth factor phenotype results from at least one vaccinia virus growth factor gene containing a substitution of nucleic acid sequence.

39. (New) The composition of Claim 29, wherein said exogenous nucleotide sequence is selected from the group consisting of tumor suppressor genes, cytotoxic genes, cytostatic genes, cytokines, suicide genes, and antigen encoding genes.

40. (New) The composition of Claim 39, wherein said tumor suppressor gene is selected from the group consisting of WT1, p53, p16, Rb, and BRCA1.

41. (New) The composition of Claim 28, wherein said vaccinia virus expression vector is produced by a virus particle containing a virus genome, wherein expression of said genome produces a vaccinia virus with a negative thymidine kinase phenotype and a negative vaccinia virus growth factor phenotype.

42. (New) The composition of Claim 28, wherein said vaccinia virus expression vector is constructed such that the gene for *E. coli lacZ* is inserted into the thymidine kinase (TK) or virus growth factor (VGF) site.

43. (New) The composition of Claim 28, wherein said vaccinia virus expression vector is constructed such that the gene for enhanced green fluorescent protein (EGFP) is inserted into the thymidine kinase (TK) or virus growth factor (VGF) site.

44. (New) The composition of Claim 28, wherein said vaccinia virus expression vector is of the WR strain.